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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,912	03/05/2002	Richard R. Bott	GC724	9189
7590 09/27/2004				
JANET KAISER CASTANEDA		EXAMINER		
GENENCOR INTERNATIONAL, INC.		STEADMAN, DAVID J		
925 PAGE MILL ROAD		ART UNIT		
PALO ALTO, CA 94304-1013		PAPER NUMBER		
		1652		

DATE MAILED: 09/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/091,912

Applicant(s)

BOTT ET AL.

Examiner

David J Steadman

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 July 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,9,19 and 27-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,9,19 and 27-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 March 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Application

- [1] Claims 1-2, 9, 19, and 27-38 are pending in the application.
- [2] Applicants' amendment to the claims, filed July 15, 2004, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.
- [3] Applicants' amendment to the specification, filed July 15, 2004, is acknowledged.
- [4] Applicants' arguments filed July 15, 2004 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.
- [5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Specification/Informalities

- [6] In view of applicants' amendment to the specification, the objections to the specification as set forth in items [10]-[12] of the Office action mailed January 29, 2004, are withdrawn.

Claim Objections

- [7] In view of applicants' amendment to the claims, the objections to claims 10 and 13-14 as set forth in items [13]-[14] of the Office action mailed January 29, 2004, are withdrawn.

Art Unit: 1652

[8] Claims 1, 19, 27-28, 30-31, and 33-38 are objected to as the identification of amino acid residues/positions is inconsistent. For example, claim 1 identifies an amino acid position by reciting "positions corresponding to sites 194 and 192," however, claim 19 identifies amino acid positions using the format "Ile 192." While it is noted that there is no ambiguity as to the amino acid that is being identified using either format, it is suggested that applicants maintain consistency in identifying amino acids throughout the claims.

[9] Claims 1 and 28 are objected to as the numbering of amino acids is not in increasing numerical order. In the interest of clarity, it is suggested that applicants recite the numbering of amino acid positions in increasing numerical order by, for example, replacing "sites 194 and 192" with "sites 192 and 194."

[10] Claims 2 and 29 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. There is no indication in the specification that the polypeptide of claim 2, *i.e.*, the polypeptide of claim 1 isolated from *P. mendocina*, is any different from the polypeptide of claim 1. Thus, the polypeptide of claim 2 does not further limit the polypeptide of claim 1.

[11] Claim 37 is objected to in the recitation of "Phy 194." This is an obvious spelling error and it is suggested that applicants replace "Phy 194" with "Phe 194." Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

[12] In view of applicants' amendment to the claims, the rejection of claims 2-3, 9-10, 12-15, 19, and 29 under 35 U.S.C. 112, second paragraph, as set forth in item [15] of the Office action mailed January 29, 2004 is withdrawn.

[13] The rejection of claim 27 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "stability" is maintained for the reasons of record as set forth in item [15] part [c] of the Office action mailed January 29, 2004 and for the reasons stated below.

[14] RESPONSE TO ARGUMENTS: Applicants argue that, in regards to claim 27, there is no comparative language as the term "thermostable" is known to those of skill in the art. Applicants' argument is not found persuasive.

It is noted that there is no recitation of "thermostable" in claim 27. Instead, claim 27 is rejected in the recitation of "stability" as it is unclear as to what "stability" is being increased, e.g., temperature, pH, or salt stability. It is suggested that applicants clarify the meaning of the claim.

[15] The rejection of claim 28 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "thermostable" is maintained for the reasons of record as set forth in item [15] part [d] of the Office action mailed January 29, 2004 and for the reasons stated below.

While applicants do not formally respond to the rejection of claim 28, it appears that applicants' argument directed to claim 27 is relevant to the instant rejection.

Art Unit: 1652

Applicants argue that there is no comparative language as the term "thermostable" is known to those of skill in the art. Applicants' argument is not found persuasive.

While applicants assert the term "thermostable" is known to those of skill in the art, it should be noted that no attempt has been made to state the art-recognized definition of the term in order to clarify its use. Instead, one of skill in the art recognizes that the term, because it is a relative term, has a plurality of meanings because it is unclear as to what the thermostability of the claimed polypeptide is being compared. Is it being compared to a corresponding wild-type cutinase? Or the thermostability of some other polypeptide? It is unclear from the claims and the specification as to what the thermostability of the claimed cutinase is being compared and it is suggested that applicants clarify the claim.

Claim Rejections - 35 USC § 112, First Paragraph

[16] The written description rejection of claims 1-2, 9, 19, and 27-38 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth at item [16] of the Office action mailed January 29, 2004, and for the reasons stated below.

[17] RESPONSE TO ARGUMENTS: Applicants argue Table 1 at page 14 of the specification describes additional species of the claimed genus of cutinase variants with substitutions at 41 different positions. Applicants' argument is not found persuasive.

It should be noted that the claims are not limited to those variants disclosed at Table 1 of the specification. In view of the recitation of, e.g., "cutinase variant comprising substitution" (claims 1 and 28), the claims have been construed in

Art Unit: 1652

accordance with MPEP 2111 as meaning a cutinase having a substitution at the recited positions *and any other position(s)* within the recited reference sequence. This interpretation is supported by applicants' argument that Table 1 discloses additional species of cutinase variants – variants that have substitutions other than mutations at positions 192, 194, and 219. As such, the genus of claimed cutinase variants encompasses a widely variant genus with respect to the amino acid sequences of the claimed genus of cutinase variants, including any variant having any combination of substitutions of the reference sequence of SEQ ID NO:2. In this case, the representative species of SEQ ID NO:2 having substitutions at positions consisting of 192, 194, and 219 fail to represent the entire genus of claimed variant cutinases. Consequently, the claimed genus of cutinase variants is not described by the specification.

[18] The scope of enablement rejection of claim(s) 1-2, 9, 19, and 27-38 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth at item [17] of the Office action mailed January 29, 2004 and for the reasons stated below.

[19] RESPONSE TO ARGUMENTS: Applicants argue Table 1 at page 14 of the specification discloses additional working examples of the claimed cutinase variants and enables many cutinase variants in addition to those recited in the claims. Applicants' argument is not found persuasive.

The examiner maintains the position that the specification, while being enabling for SEQ ID NO:2 having substitutions at positions consisting of 192, 194, and 219, does not reasonably provide enablement for the broad scope of claimed cutinase variants. In

Art Unit: 1652

response to applicants' argument, it should be noted that the claims are not limited to those variants disclosed at Table 1 of the specification. As stated above, in view of the recitation of, e.g., "cutinase variant comprising substitution" (claims 1 and 28), the claims have been construed in accordance with MPEP 2111 as meaning a cutinase having a substitution at the recited positions *and any other position(s)* within the recited reference sequence. This interpretation is supported by applicants' argument that Table 1 discloses additional cutinase variants – variants that have substitutions other than mutations at positions 192, 194, and 219. As such, the claims broadly encompass a vast number of cutinase variants without providing guidance for making the entire scope of such variants. As previously stated (see pp. 12-13 of the Office action mailed January 29, 2004), and undisputed by applicants, without such guidance, it is highly unpredictable as to which mutation(s) in addition to positions 192, 194, and/or 219 can be made with an expectation of maintaining a polypeptide having the desired activity. Moreover, screening for the entire scope of such variants is not routine. As such, the specification fails to enable the full scope of claimed cutinase variants and undue experimentation is required to make all cutinase variants as broadly encompassed by the claims.

Claim Rejections - 35 USC § 102

[20] In view of applicants' arguments and the amendment to the claims, the rejection of claims 1-3, 9, 12, and 28-29 under 35 U.S.C. 102(b) as being anticipated by

Art Unit: 1652

Poulouse et al. as evidenced by Boston et al. as set forth at item [19] of the Office action mailed January 29, 2004 is withdrawn.

Claim Rejections - 35 USC § 103

[21] Claim(s) 1-2, 9, and 27-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Poulouse et al. (US Patent 5,352,594; cited by the examiner in a previous Office action). The claims (in relevant part) are drawn to variants of *P. mendocina* cutinase having mutation at positions corresponding to amino acids 192 or 194 and 219 of SEQ ID NO:2 and optionally wherein the variant has enhanced properties. It is noted that claims 1 and 28 have been broadly interpreted in accordance with MPEP 2111 as meaning a cutinase having a substitution at the recited positions *and any other position(s)* within the recited reference sequence as explained in detail above.

Poulouse et al. teach variants of a *P. mendocina* lipase (columns 3-5) having substitution of Ser205 (corresponding to amino acid 219 of SEQ ID NO:2) with various amino acids (see columns 11-14). Poulouse et al. further teach that the catalytic triad of *P. mendocina* lipase is Ser126, His206, and Asp176 (column 5, middle) – corresponding to amino acids Ser140, His220, and Asp190 of SEQ ID NO:2 – and that replacement of amino acid within about 6 amino acids N- or C-terminal to a catalytic amino acid will lead to an increase or decrease in the perhydrolysis/hydrolysis ratio and the kinetic constants of the enzyme (column 5, lines 41-57). Poulouse et al. teach that in order to obtain an enzyme with the best ratio or substrate specificity in a desired

Art Unit: 1652

direction, more than one amino acid substitution can be made (column 6, lines 41-45) and provide an example as follows: a Gly205-Thr207 double mutant (corresponding to a 219-221 double mutant of SEQ ID NO:2) had an improved specific activity over a single Gly205 mutant (columns 15-16). Poulouse et al. provide methods for generating mutations in the sequence of *P. mendocina* lipase, including double mutants (columns 7-8) and methods for screening mutants for desired properties/activities (columns 8-9).

Therefore, it would have been obvious to one of ordinary skill in the art to mutate position 178 or 180 (corresponding to amino acids 192 or 194 of SEQ ID NO:2) of *P. mendocina* lipase with any of the twenty common amino acids by saturation site-directed mutagenesis and to optionally further mutate position 205 of *P. mendocina* lipase (corresponding to amino acid 219 of SEQ ID NO:2) with any of the twenty common amino acids by saturation site-directed mutagenesis. One would have been motivated to mutate position 178 or 180 of *P. mendocina* lipase and to further mutate position 205 of *P. mendocina* lipase in order to mutate an amino acid within 6 amino acids of a catalytic amino acid (Asp176 of *P. mendocina* lipase) to obtain a polypeptide having the improved characteristics as described by Poulouse et al. One would have a reasonable expectation of success for mutating position 180 of *P. mendocina* lipase and to further mutate position 180 of the *P. mendocina* lipase position 205 mutants of Poulouse et al. because of the results of Poulouse et al. Therefore, claims 1-2, 9, and 27-38, drawn to the mutant *P. mendocina* cutinase as described above would have been obvious to one of ordinary skill in the art.

Art Unit: 1652

[22] It is noted that Poulouse et al. do not teach that their suggested *P. mendocina* lipase variants have enhanced stability, thermostability or enhanced polyesterase activity. However, these properties would have been inherent features of the variants as suggested by Poulouse et al.

[23] RESPONSE TO ARGUMENTS: Applicants argue that during the development of the instant invention, the best-performing variants as described by Poulouse et al. were insufficient to meet the need addressed in the present application. Applicants' argument is not found persuasive.

The claimed variants are not limited to variants having mutation at specific amino acids and/or having an enhanced activity relative to a wild-type *P. mendocina* cutinase. Poulouse et al. clearly suggest altering position 178 or 180 and optionally position 205 of *P. mendocina* lipase. As such, the reference of Poulouse et al. makes obvious the claimed cutinase variants.

[24] It should be noted that, based upon applicants' arguments, it would appear that applicants were aware of the reference of Poulouse et al. at the time of the invention (see particularly page 13 of the response filed July 15, 2004). However, there is no disclosure of this reference on Form PTO-1449 filed August 29, 2003. Applicants are reminded of their duty to disclose information material to patentability according to 37 CFR 1.56.

Conclusion

[25] Status of the claims:

Art Unit: 1652

- Claims 1-2, 9, 19, and 27-38 are pending.
- Claims 1-2, 9, 19, and 27-38 are rejected.
- No claim is in condition for allowance.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.


David J. Steadman, Ph.D.

Primary Examiner

Art Unit 1652

09-20-04